REMARKS

Claims 1, 2, 4-10 and 12-15 are pending in the instant application. Claims 1, 2, 4-10 and 12-15 have been rejected. Reconsideration is respectfully requested in light of the following remarks.

I. Rejection of Claims Under 35 U.S.C. 102(b)

Claims 1 and 2 have been rejected under 35 U.S.C. 102(b) as being anticipated by Kalff-Suske et al. (1999). The Examiner suggests that this reference discloses antisense oligonucleotides 8 to 50 nucleobases in length that specifically hybridize with and inhibit expression of human glioma associated oncogene-3 *in vitro*. Applicants respectfully disagree with the Examiner's conclusions regarding this reference.

Kalff-Suske et al. (1999) disclose that mutations of glioma-associated oncogene-3 are directly involved in Greig's cephalopolysyndactyly, Pallister-Hall syndrome and post-axial polydactyly. Although this reference teaches 9 primers, four of which hybridize to SEQ ID NO: 3, these primers do not specifically hybridize with and inhibit expression of human glioma associated oncogene-3. These primer pairs were used to perform a technique called single-strand conformation analysis (SSCA). The authors

cite the method as being disclosed in reference 15 of their paper (Wild et al. 1997). Review of this method shows clearly that the primers were used in a PCR-based mutation assay and would not have worked in that assay if they had been operating to reduce gene expression as claimed by the Examiner. In fact, the opposite is true. The primers were used to amplify the variants. Therefore, contrary to the Examiner's suggestion, this reference does not teach or suggest antisense compounds that are capable of inhibiting expression of human glioma associated oncogene-3 as claimed. Therefore, this reference fails to teach the limitations of the claims. MPEP 2131 states that in order to anticipate a claim the reference must teach each and every limitation of the claim. Accordingly this reference cannot anticipate claims 1 and 2 as it fails to teach the limitations of the claims. Withdrawal of this rejection is therefore respectfully requested.

II. Rejection of Claims Under 35 U.S.C. 103(a)

Claims 1, 2, 4-10 and 12-15 have been rejected under 35 U.S.C. 103(a) as being unpatentable over either of Ruppert et al. (1990) and Kalff-Suske et al. (1999), in view of Milner et al. (1997) and Baracchini et al. (US Patent 5,801,154). The Examiner suggests that it would have been *prima facie* obvious to one of ordinary

skill to design and use antisense molecules for inhibition of glioma-associated oncogene-3 expression since the sequence encoding the gene was known (Ruppert et al. and Kalff-Suske et al.), that Kalff-Suske et al. teach antisense compounds targeted to human glioma associated oncogene-3, that methods of screening for antisense have been taught by Milner et al., and Baracchini et al. teach modification of antisense as claimed. The Examiner suggests one of skill would have been motivated to do so by the teachings of Baracchini et al. and Milner et al. Applicants respectfully disagree with the Examiner's suggestions regarding these references.

Ruppert et al. (1990) disclose the cloning and mapping of human glioma-associated oncogene-3 and its link to a chromosome region involved in Pallister-Hall syndrome. While disclosing the sequence of the gene, nowhere does this reference teach or suggest antisense compounds of any type targeted to glioma-associated oncogene-3 nucleic acid molecules as claimed. Therefore, this primary reference fails to teach the limitations of the claims.

Kalff-Suske et al. (1999) disclose that mutations of glioma-associated oncogene-3 are directly involved in Greig's cephalopolysyndactyly, Pallister-Hall syndrome and post-axial

polydactyly. As discussed *supra*, although this reference teaches primers for the gene, this reference fails to teach antisense compounds capable of inhibiting expression of human glioma associated oncogene-3. Therefore, this primary reference also fails to teach the limitations of the claims as filed.

The secondary references cited fail to overcome the deficiencies in teaching of the primary references.

Milner et al. teach a method for identifying antisense oligonucleotides using optimization techniques where the antisense oligonucleotides have 1-17 bases and target sequences of a gene. However, nowhere does this paper teach or suggest antisense oligonucleotides 8 to 50 nucleobases in length targeted to glioma-associated oncogene-3.

Baracchini et al. (US Patent 5,801,154) teach methods of modifying antisense oligonucleotides to enhance activity. However, nowhere does this patent teach or suggest antisense oligonucleotides 8 to 50 nucleobases in length targeted to glioma-associated oncogene-3 nucleic acid molecules.

To establish a *prima facie* case of obviousness, three basic criteria must be met. MPEP 2143. First, there must be some suggestion or motivation, either in the references themselves or in

the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art must teach or suggest all claim limitations. Clearly, the combination of prior art cited fails to teach or suggest the limitations of the claims as filed, which claim antisense compounds targeted to glioma-associated oncogene-3 that are capable of inhibiting expression of the gene, and thus cannot render the instant claimed invention obvious. Mere teaching of the sequence of a gene and its function, and then teaching of antisense technology in general to a completely other gene target, or primers that may have a sequence overlap, does not provide one of skill with the expectation of success in developing antisense targeted to a specific gene that does indeed inhibit expression of the gene. The limitations of the claims as filed, which specify antisense compounds targeted to human glioma-associated oncogene-3 (SEQ ID NO: 3) that are capable of inhibiting gene expression, are not taught or even suggested by any of the references individually or when combined. Therefore, the limitations of the claims as amended clearly are not taught or suggested by the combination of prior art references, nor is any expectation of successful use of such

antisense compounds provided by the combination of prior art. It is only with the specification in hand that one of skill would understand that antisense compounds targeted to glioma-associated oncogene-3 could be used to inhibit expression of this gene. Thus, the combination of prior art cited cannot render the instant claimed invention obvious. Withdrawal of this rejection is therefore respectfully requested.

III. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

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